

### **REMARKS**

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, Claims 1-4 and 9-13 will remain pending in the application. Applicants have canceled Claims 5-8 and added Claims 9-13. These changes do not introduce new matter, and their entry is respectfully requested.

In the Office Action of February 13, 2003, the Examiner set forth a number of grounds for rejection. These grounds are addressed individually and in detail below.

#### **Claim Objection**

Claim 5 stands objected for containing a plurality of method steps but not indentations to separate the steps. Claims 6 and 7 stand objected for the reasons set forth on page 3 of the Outstanding Office Action.

Applicants have canceled Claims 5-7. This ground of objection is now moot.

#### **Rejections Under 35 U.S.C. § 112, second Paragraph**

Claims 5-8 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the reasons set forth on pages 3-4 of the Office Action.

Claims 5-8 have been canceled, and the newly added Claims 9-13 clearly define the present invention. These grounds of rejection have been obviated and thus, withdrawal of the 35 U.S.C. § 112, second paragraph, rejection is respectfully requested.

**Rejections Under 35 U.S.C. § 103**

Claims 5-7 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Bekkaoui et al. (US 613,6553) in view of Ryffel et al (Gene, 94 (1990) 137-138) for the reasons set forth on pages 5-7 of the Office Action. Claim 8 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Bekkaoui in view of Ryffel, and further in view of Ishiguro et al for the reasons set forth at page 7 of the Office Action. The Examiner alleges that Bekkaoui teaches a probe useful for the detection of MRSA. The Examiner further indicates that SEQ ID NO:4 of Bekkaoui overlaps with SEQ ID NOS: 20 and 21 of the instant invention, and therefore, it would have been *prima facie* obvious to one skilled in the art to have used the sequence taught by Bekkaoui in the instant invention. The Examiner further alleges that Ryffel provides the full length sequence of the *mecA* gene from three different methicillin resistant *Staphylococci*, one skilled in the art would have been motivated to select primers within the region conserved among different *mecA* genes. Claims 5-8 have been canceled and replaced with new Claims 9-13. Accordingly, Applicants respectfully traverse the rejection.

To establish a *prima facie* case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." In re Wilson, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970).

The disclosed invention is directed to a method for detecting MRSA with an RNA amplification process comprising the synthesis of cDNA from an RNA template, the digestion of RNA-DNA hybrid, the second strand synthesis of the cDNA, and the transcription of an RNA product from the double-stranded cDNA. Independent Claim 9, as amended, provides two modes of operation. In the first mode, the first primer includes the RNA polymerase promoter

sequence and the reaction mixture contains a cleaving oligonucleotide probe (page 10, line 20 to page 12, line 4). In the second mode, the second primer includes the RNA polymerase promoter sequence and the reaction mixture does not contain a cleaving oligonucleotide probe (page 12, line 4 to page 13, line 15). The present invention also discloses the specific primer/probe combinations for the detection of MRSA.

In contrast, Bekkaoui generally describes a detection method using an RNA amplification process involving reverse transcription. Bekkaoui does not disclose the primer combination claimed in the present invention. Ryffel simply discloses full length sequences of the *mecA* genes from several methicillin resistant *Staphylococci*. Neither Bekkaoui nor Ryffel teaches or suggests the use of a cleaving probe in the RNA amplification process. Consequently, one skilled in the art would not be able to produce the present invention based on Bekkaoui and Ryffel without undue experimentation. Accordingly, for this reason alone, the instant invention is patentable over Bekkaoui and Ryffel.

In addition, when applying 35 U.S.C. § 103, the Examiner is also required to adhere to the following tenets of patent law: (1) The claimed invention must be considered as a whole; (2) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (3) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (4) Reasonable expectation of success is the standard with which obviousness is determined. (MPEP, 2141.01).

Furthermore, the CAFC in In re Sang Su Lee states teaching of references can be combined only if there is some suggestion or incentive to do so. In re Sang Su Lee (Fed. Cir. January 18, 2002) (quoting ACS Hosp. Sys., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577 (Fed. Cir. 1984)). Particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in

the manner claimed. *Id.* Furthermore, the Court states even when the level of skill in the art is high, the Board must explain the reasons one of ordinary skill in the art would have been motivated to select the references and to combine them to render the claimed invention obvious. *Id.*

In this case, Bekkaoui generally describes a detection method using an RNA amplification process involving reverse transcription. However, the Examiner agrees that Bekkaoui failed to teach or suggest the primer sequences that are required for the effective amplification of the *mecA* gene of MRSA.

Furthermore, the probe of Bekkaoui having SEQ ID NO:4 is an RNA-DNA chimeric probe containing a stretch of four ribonucleotides flanked by deoxyribonucleotide sequences on both ends (Col 17, line 18). It is used for the purpose of annealing to the target DNA molecule to form a double-stranded complex so that the RNA portion of the RNA-DNA hybrid can be cleaved by ribonuclease H to release the labeled DNA probe.

In contrast, the primers of the instant invention containing SEQ ID NO:20 or 21 (which the Examiner says overlaps with SEQ ID NO:4 of the reference) are used as primers to initiate DNA synthesis. The probe in Bekkaoui and the primers in the instant invention are intended and used for different purposes. Accordingly, it would not be obvious for one skilled in the art to use the same sequence in the two distinct applications.

With respect to the Examiner's contention that Ryffel provides the full length sequence of the *mecA* gene from three different methicillin resistant *Staphylococci*, and that one skilled in the art would have been motivated to select primers within the region conserved among different *mecA* genes, Applicants respectfully submit the disclosure of full length sequence of a gene does not automatically provide primer/probe sequences for a particular application. Extensive optimization is often required to identify the particular sequences suitable for a particular

application. Moreover, SEQ ID NOS:19, 21, 23, 24 and 25 are within regions that are not conserved among different *mecA* genes. Thus, it is not obvious to one skilled in the art to derive the present invention from the prior art of record.

Therefore, the references of Bekkaoui and Ryffel do not support a *prima facie* case of obviousness. The grounds for this rejection have obviated and withdrawal of the 35 U.S.C. § 103 rejection is respectfully requested.

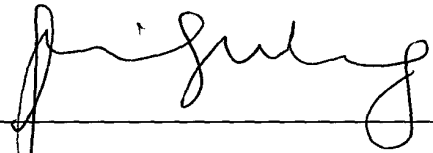
### CONCLUSION

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to contact Ping Wang, M.D. (Reg. No. 48,328) at the telephone number listed below.

Respectfully submitted,

PIPER RUDNICK LLP

A handwritten signature in black ink, appearing to read "S. Kelber", is written over a horizontal line.

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